SOME CAUSATIVE FACTORS OF PULMONARY TUBERCULOSIS

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In discussing before you the etiology—the cause—of pulmonary tuberculosis, which accounts for 87 percent of all the deaths from tuberculosis in the United States, I am more at my ease than I could be with any other topic connected with pulmonary tuberculosis, for no matter how bizarre my statements may be, I might quote opinions and even experiments to prove that they are right.

As time flies on, we are all impressed by the fact that many utterances relating to this subject, often ipse dixit in character, are sustained not by proof but by weight of authority. In fact, we have had thrust upon us so many half truths, that if we seriously consider the whole problem to-day we find that students of pulmonary tuberculosis are in complete accord upon only one fact, established thirty-nine years ago, namely, that pulmonary tuberculosis is due always to the presence of tubercle bacilli in the lungs. At first thought, the etiologic chain seemed complete. The tubercle bacilli grew and multiplied in the lung, producing, as the disease progressed, ulceration into the bronchi, through which bacilli escaped into the open by means of the sputum, which was formerly deposited much more freely and carelessly upon floor, platform, or sidewalk than it is to-day. From these places the bacilli somehow gained entrance into the body of a new host. So, to prevent the spread of the disease this cycle must be broken at some point, which in the earlier days seemed simple enough to do.

It was but natural for Cornet to attempt to prove that the usual method of transference from man to man is through the inhalation of the fine particles of dried tuberculous sputum wafted about as dust.

For years this was accepted as the usual means of inanimate transmission. But patients, Flügge said, when they cough emit a spray of coarser and finer and almost impalpable particles of sputum that fly to a distance of three to four feet from the mouth and may remain suspended

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in the air for about a half-hour. This, as the usual method of transfer-
ence, was for him far more important than dust. More recently these
so called inhalation methods of infection have been questioned as far as
they can be considered the usual method of infection. Krause would
emphasize the importance of raw sputum, contaminating the hands of
young children through balls, hoops, tops, etc., used in play upon our
streets, while Cumming would emphasize that eating utensils, particu-
larly spoons, which our younger children use almost exclusively, are in
his opinion the chief conveyers of infection, for ordinary washing by no
means sterilizes them.

However it occurs, we know that a large proportion of the urban
population, at least, harbor the tubercle bacillus by the time they reach
puberty. This might be stated as a second uncontroversial fact.

But from this time on we again encounter divergent views. Some
would have us believe that all pulmonary tuberculosis is due to the fur-
ther progression of a childhood infection and that adults are practically
never reinfected. On the other hand there are those who maintain that
while this does hold true in a certain proportion, say in 50 per cent of the
cases of adult pulmonary tuberculosis, in the other 50 per cent pulmonary
tuberculosis is due to adult infection. In either case infection is not
synonymous with disease, and it must be explained how so large a pro-
portion of infected individuals never develop frank disease. Here it
seems to me that we must separate, as clearly as possible (which is not
often done), those causative factors which bring about infection from those
which bring about the development of infection into clinical disease.
It may be stated briefly at this point that any circumstance that upsets
a bodily balance which has prevented tuberculous infection from advanc-
ing into tuberculous disease is, of course, a causative factor. I refer
among others, to overwork, poor hygienic surroundings, poor food and
certain diseases.

I have mentioned two basic facts that we can all agree upon: first,
without the presence of the tubercle bacilli in the lungs there can be no
pulmonary tuberculosis; and, second, by the age of puberty a large
majority of children (70 per cent) harbor or have harbored the tubercle
bacilli in their bodies, more particularly if they dwell in cities. By the
age of twenty-five somehow all have been infected with tubercle bacilli.

I should like to divide my further remark into a discussion (1), of
the tubercle bacillus, the parasite that causes the disease and (2), of the
host, the human being, that is diseased.
THE PARASITE: THE TUBERCLE BACILLUS

This suggests a brief consideration of the tubercle bacillus, the parasite, which brings about infection and later, under certain conditions, disease. This germ has been held to have feeble powers of attack, if I may so term it, but great powers of resistance, thanks to its waxy framework. It is nonmotile, and depends upon the bodily functions to transport it within the body and upon air currents and inanimate objects for movement without the body. It was formerly thought to be ubiquitous but recently studies have not upheld this view. However this may be, all of us sooner or later come in contact with the tubercle bacillus and many of us meet it frequently. It is of interest to see where it lurks outside the body and to trace if possible its path from cow or man to the ill fated individual who develops pulmonary tuberculosis.

The bovine tubercle bacillus. The danger of tuberculous meat is practically nil; but the danger of milk containing bovine tubercle bacilli is more real, and can be roughly estimated in two ways: first, by noting what percentage of human beings suffer from bovine tuberculosis, and, second, by observing the effect of contaminated milk upon individuals who have imbibed it.

Figures collected in 1911 by Park and Krumwiede show that in 1224 cases in which the type of tubercle bacillus was determined, the bovine tubercle bacillus caused 4.3 per cent (that is, one case in 24 examined) of pulmonary tuberculosis occurring in children and infants under five years of age, none in patients from five to sixteen years (11 cases), and one in 645 cases of adult pulmonary tuberculosis. In other words, bovine tubercle bacilli caused pulmonary tuberculosis in only 2 of 680 cases, less than one-third of one per cent, a figure that appears almost negligible. In a collected study of the type of the bacilli in the sputa in 938 patients with pulmonary tuberculosis, at least three were found to be of bovine origin (Griffith), one was doubtful and two were mixed. In any case, far less than 1 per cent and in all probability less than one-half of 1 per cent were thus due to the bovine tubercle bacillus. Do not misunderstand me: bovine tubercle bacilli produced the disease that killed nearly one-fourth (23 per cent) of the 280 cases of all forms of tuberculosis occurring under five years of age, slightly more (24 per cent) in the 153 cases between the fifth and sixteenth year of life, but only 1.3 per cent in adults. In this group of figures pulmonary disease occurred in 82 per cent of the cases in adults, in 7 per cent between five and sixteen years, and about in 9 per cent of children under five years.
Two years later (1913) Kossel collected the figures of various observers in all countries and found that in 832 cases of pulmonary tuberculosis, three were due to bovine, two to bovine and human, and one was badly defined, or in other words, in over 99 per cent (99.3 per cent) of all cases of chronic pulmonary tuberculosis, the disease was caused by human tubercle bacilli. From these figures, then, the importance of bovine tubercle bacilli in pulmonary tuberculosis in man is at the most but slight.

The mutation of bovine tubercle bacilli. The mutation or transformation of the bovine into the human type of tubercle bacillus has been frequently suggested. From the figures I have mentioned it can be seen that up to puberty bovine tubercle bacilli are frequently found, but after this age they occur so rarely that some have suggested that they are transformed into the human type. This change of mutation has never been proved. I have never been able to find any study which determined whether or not a bovine infection persisted before, through and after puberty. The infinitesimal additions of certain substances, that bring about marked changes in colloidal states, suggest that at puberty certain changes might occur in the bodily tissues that render them no longer suitable for growth of bovine and possibly more suitable for the growth of human tubercle bacilli. This is in part borne out by the fact that bovine bacilli grow less readily than human bacilli upon artificial media and require slightly less acidity, or lower hydrogen ion concentration, as it is termed to-day. Thousands of adults must drink tuberculous milk daily and while thus exposed they apparently almost never develop bovine disease.

It is common knowledge that bovine tubercle bacilli do occur in cow's milk and in some specimens it has been estimated that one-half million tubercle bacilli are contained in one teaspoonful of milk. It has been found that 16 per cent of the specimens of milk examined in New York (in 1910) contained tubercle bacilli; 10.5 per cent in Chicago (in 1910); 7 per cent in Washington; 22 per cent in London; and 20 per cent in Edinburgh. In Berlin 619 persons (284 children, 335 adults) who had drunk raw milk from cows with tuberculosis of the udders were studied (A. Weber). Only 2 children were clinically tuberculous (both had cervical adenitis). Of 18 children (9 under two years, 8 from two to five years and one more than five) exposed in a similar way, only one became clinically tuberculous (it also had cervical adenitis); and but 4 reacted to the ophthalmic tuberculin test. In fact, in regard to the danger of tuber-
culous milk we are led to conclude that only when children are fed constantly with milk containing large quantities of tubercle bacilli is the danger great, and as milk bought in large cities comes usually from many herds, the quantities of tubercle bacilli are usually not large. These facts, however, do not relieve us of the necessity of obtaining milk for our children from tuberculin tested herds or of pasteurizing it before use, for from 8 to 10 per cent of all tuberculosis deaths in children are due to the bovine tubercle bacillus.

The human tubercle bacillus. Now if we can exclude the bovine tubercle bacillus as the cause of chronic pulmonary tuberculosis in adults, and I think the figures I have presented to you enable us to do so, we can concern ourselves entirely with the human type. In other words, practically every patient with pulmonary tuberculosis has been infected either directly or indirectly by another patient. How do these bacilli pass from person to person?

We know that the sputum of patients with advanced disease may contain enormous numbers of bacilli. Professor Nuttall of Cambridge, formerly connected with this University, estimated that the sputum could contain as many as one to four billions of tubercle bacilli in twenty-four hours, and Heller estimated that a patient could expectorate over seven billions of tubercle bacilli in the same time, though all of these are probably not alive. With the prevalence of tuberculosis which has existed for years, along with the former belief that tuberculosis was hereditary and not contagious, and with the careless disposal of the sputum in use for years, it seems almost incredible that many more did not succumb to pulmonary tuberculosis, if the tubercle bacilli in the sputum could be distributed as some would have us believe.

The danger of dust. I have referred to Cornet's work which he believed went to show that tubercle bacilli were carried from man to man by means of particles of dust. The patient spits upon the sidewalk, upon the floor perchance, and the unwitting carrier bears the bacilli on shoes or skirts into the house, there to deposit them upon the rugs or carpets. The sputum dries and, according to this theory, is ground into dust which the careful housewife cannot bear to see at rest. So literally she dusts not only the floors, the furniture, but also the lungs of those who dwell therein. On a tiny particle of dust, visible only when it dances in the sunbeam, ride perchance twenty or more tubercle bacilli along the

* It is of interest to note in passing that many housewives contract tuberculosis but the percentage of housewives form a large part of the female population.
various air currents, to find finally a resting place in a tiny ramification of a bronchial tube, deep in the interior of the lung. Here, in some instances, the bacilli proliferate; some would have us believe in the air passage itself; others (and this is more probable) only after they have penetrated the mucous membrane and gained access to the intrapulmonary masses of lymph tissue. Their growth and the resultant destruction and compression of pulmonary tissue ultimately bring about clinical pulmonary tuberculosis.

That bacilliferous sputum has been in the past and still is widely distributed on our sidewalks, on platforms, on the floors of public buildings and elsewhere, cannot be denied. Such sputum can be used to infect guinea pigs. But aside from this what do we know of the existence of human tubercle bacilli outside the body? Innumerable experiments have been performed to show how long the tubercle bacillus can resist light, air and drying. Direct sunlight or sunshine is supposed to kill tubercle bacilli in thin layers of sputum in a few hours (four to six), while indirect sunlight may require several days to do so. Fresh air, even in the absence of sunlight, has caused their death in a few days; combined with sunlight it would work more quickly. Dessication is also injurious. When in masses of mucus, however, tubercle bacilli may be protected from the effects of light and of drying which render the mucus a tough or hard mass. So tubercle bacilli deposited upon our streets in large masses of sputum, especially in coarse dust and sand, may resist for days these destroying forces. It is interesting to consider then what happens to a mass of sputum which is trodden under foot on a sidewalk. While contaminated shoes may track it into the house, the mere fact that it has been spread out over a fairly wide area renders the tubercle bacilli that remain upon the street far less resistant, and in my opinion greatly hastens their death. I can conceive how a shoe contaminated by such sputum several blocks from home can be of danger or a source of infection, particularly for young children who play about their elders.

Mr. Petroff, Dr. Pesquera and I poured some sputum containing innumerable tubercle bacilli on a board, trod upon it and then trod on and wiped, so to speak, our shoes on a piece of carpet. After some hours the carpet was placed in a small box containing several guinea pigs, and a stiff, rotary brush attached to a motor was set in motion and kept running for some hours on several different days. None of the guinea pigs became infected.
Samples of dust from many locations, both indoors and out, have been searched for human tubercle bacilli and injected at times into guinea pigs, all with varying results (18 per cent to 48 per cent were positive (Cornet)), but experiments made with the dust that leaves the floor after ordinary dry sweeping, that is, with the dust we ordinarily inhale, have proved it infectious far less often (8 per cent). It may be stated that, when tuberculous sputum becomes dried and ground into dust out-of-doors, the tubercle bacilli are so weakened that they are of little danger or else are killed. House dust may be much more dangerous and to-day many hold that tuberculosis is practically always contracted indoors. The statement that pulmonary tuberculosis is a house disease must embrace this fact; but it must also be remembered that families that hover about the poverty line often sink into the same wretched living quarters. Under these circumstances lack of food may be as important as exposure to the infectious dust left by a previous occupant. Such conditions, it appears to me, have often less to do with infection than with the development of disease from previous infection.

Mr. Petroff, Dr. Pesquera and I also tried to find tubercle bacilli outside the body in Saranac Lake and at the Trudeau Sanatorium. Two rooms occupied by patients with violent coughs, both of whom have since died, were carefully examined in regard to the dust upon the floor, the walls, the bed table and the chair, but no tubercle bacilli were found either by staining or by inoculation of guinea pigs. This confirmed the finding of a former assistant, who, hoping to show that tubercle bacilli were present in the dust of a room in the infirmary at Trudeau, occupied by a patient with numerous tubercle bacilli in his sputum and an explosive violent cough, inoculated the dust into a guinea pig with negative results. Having found no tubercle bacilli in the dust of rooms by the use of swabs, we constructed a glass chamber, just large enough to hold a guinea pig and attached it to a vacuum cleaning apparatus which drew the dust of the room past the guinea pig for one-half hour. Guinea pigs we thought, might contract tuberculosis through inhalation when inoculation failed, but the three guinea pigs used remained free from tuberculosis. Much emphasis has been laid upon the danger from the mouth pieces of telephones, but dust collected from the public telephone at Trudeau failed to infect guinea pigs. The dust collected from a large rug in the general assembly room at Trudeau also produced no tuberculosis on inoculation.
These experiments led us to conclude that, with the prophylactic technique in use at Trudeau and Saranac Lake, the dust of rooms was no source of danger. It must be remembered, however, that if the consumptive spits upon the floor, it is very likely that the dust from the room will infect a guinea pig, which Hance proved many years ago at Trudeau. Virulent tubercle bacilli have been found in the dust of a room six weeks after the death of a consumptive, but usually at the end of six months all infectivity has gone.

The climate which stimulates us, which gives us our energy, which in short makes Americans of us, has an untoward effect upon our mucous membranes, and whether we dwell at the sea coast or on the high, dry western plateaus, we suffer more or less from catarrh and so are led to spit. The antispitting crusade has done yeoman service and as soon as the general public realizes that their health demands that sidewalks, street crossings and floors be kept free of all sputum, we shall see reductions in mortality from all respiratory diseases.

The danger of droplets of sputum. Some years ago Dr. Baldwin and I built a glass box, into which we had patients cough, and found an occasional droplet of sputum containing tubercle bacilli deposited up to a distance of about three feet. Dr. Trudeau had found tubercle bacilli in the droplets of sputum on his eyeglasses after a patient had coughed in his face. These droplets of sputum may therefore contain tubercle bacilli. It had been shown by Flügge and others that they may be sprayed to a distance of three feet or one metre from the lips of the cougher and remain suspended in the air for thirty minutes or more. These seem to me to be uncontrovertible facts. But our problem is how much danger lurks in these minute droplets.

From what has been said of the viability of tubercle bacilli, it can be seen that in such droplets they are readily exposed to the destroying influences of light, air and drying. That they can persist alive, or at least remain infectious, even in the house for more than a few hours, seems to me most unlikely, though this has been questioned.

On the other hand, however, we know that fewer tubercle bacilli in the form of a moist spray are needed to infect guinea pigs; and possibly weakened germs, thus gaining entrance into the body, may produce more or less benign pulmonary tuberculosis. It would seem to be an easy thing to cough into the face of a guinea pig and so infect it. Hoping to reproduce as much as possible the conditions under which an infant lives with a tuberculous mother, we got two of our patients at Trudeau to
fondle guinea pigs and to cough all over them during their morning pulmonary toilet. Both patients had numerous tubercle bacilli in the sputum but the guinea pigs remained free from disease. This is not an isolated experiment for others have had the same experience. Heymans, a co-worker of Flügge, had great difficulty in producing infection in guinea pigs and dogs by this method, even after hours of exposure to coughing consumptives. It should further be noted that less than 50 per cent of patients with pulmonary tuberculosis, even with tubercle bacilli in their sputum, cough out droplets containing them, and the number of tubercle bacilli contained in the droplets is only a very minute fraction of those in the sputum.

On the other hand, Hess of New York and Hamburger of Vienna would have us believe that an extraordinarily short period of contact is required to infect an infant, but fomites and infected objects may have played a greater part than was thought or known.

The danger then of droplet infection may be said to be limited to those droplets inhaled before settling upon any object and probably is much greater for infants than for older children or adults.

Common colds leading to acute bronchitis aid greatly in disseminating germs that occur anywhere in the respiratory tract. Tubercle bacilli may recur in sputum only during a cold.

The danger of contact. The spread of tubercle bacilli from man to man by direct or indirect contact has recently been emphasized. It has long been considered dangerous to shake hands with a consumptive. We selected two patients, with abundant sputum loaded with tubercle bacilli, and had them cough violently into their hands. The wash water from the hands infected guinea pigs, a point Baldwin had shown many years before. We then endeavored to see if tubercle bacilli could be transferred from hand to hand by shaking hands but were unable to do so. We repeated the experiment with large quantities of another germ (B. prodigiosus), and found that they could be passed along a chain of three or four persons by this means. It seemed to us fair to conclude that mere coughing into the hands was not enough for transmission by this method, but gross contamination of the hands by sputum, such as wiping heavily infected lips with the hands, might be. We could not spread contamination produced by coughing into the hands to another's hands by means of the door knob.

Objects that come in contact with the lips may be contaminated, for in some instances the saliva contains tubercle bacilli in considerable num-
bers. To study the danger that lurks in the kiss we had patients kiss a sterile glass dish (Petrie dish), and found the danger was greater in the early morning hours. We should have liked to have had the patients kiss a guinea pig, but we felt that even the amount of fervor that enters into kissing a glass plate might have been lacking with the guinea pig.

It has long been taken for granted that eating utensils that come in contact with the lips—glasses, cup, forks and spoons—are contaminated. This had been shown by Price and we confirmed his work. The recent epidemics of certain respiratory diseases at the training camps in various parts of the country have shown the great danger of insufficient washing of eating utensils, and particularly when insufficient and contaminated water was used.

Cumming, who has studied hand-to-mouth and utensil-to-mouth infection, has concluded that many respiratory diseases, including tuberculosis, are transmitted in this way. In fact, this he holds is the usual method of infection and he incriminates particularly the spoon. Ordinary methods of washing, he states, are insufficient to rid the spoon of tubercle bacilli, as he proves by guinea pig inoculation. Price, however, found that hand washings of utensils, followed by scalding, was enough to sterilize them. For Cumming the "control of the inanimate through universal mass action" is an epidemiologic fundamental in the control of any communicable disease.

Much has been written upon the danger of flies as a means of contamination and we, therefore, repeated the work of several observers and showed that flies fed upon tuberculous sputum were contaminated throughout with tubercle bacilli. They developed diarrhoea and the fly specks contained tubercle bacilli which caused tuberculosis when injected into guinea pigs. We then placed a receptacle of sputum containing many tubercle bacilli high up in a cage with guinea pigs and kept a dozen or more flies constantly in the cage, replacing them as they died. Specks found upon the carrots produced tuberculosis when injected into guinea pigs, but though we kept up the exposure for several weeks none of the guinea pigs developed tuberculosis. It is hardly probable that a child is often subjected to as much danger of contamination through flies as these guinea pigs were.

Infection through fomites, that is, contaminated objects, may in a few instances be the cause of infection in adults. I have in mind especially dressmakers who make over consumptives' apparel. The danger here, if the patient has undergone the present day treatment of living largely
in the open, must be very slight for the reason I have already mentioned. In the laundry the danger is greater, particularly and chiefly with the handkerchiefs which are used at times, as everyone knows, as receptacles for infectious sputum. Boiling the laundry before handling it, or, better still, the replacement of handkerchiefs by gauze in all respiratory affections would abolish this danger. The gauze is, of course, burned after use.

Tubercle bacilli have been found in books used by consumptives but the danger must be so slight as to be negligible.

It has been suggested by Krause that children of three and four years of age, put to play on the streets, come in direct contact with tuberculous sputum. Their balls, tops, hoops, fall in the gutter or roll through masses of sputum on the sidewalks. Their infected hands quickly find their way to their mouth and tuberculous infection sooner or later results. It has occurred to me that a study of the sputum deposited upon the sidewalks and elsewhere might be made in a limited locality in Baltimore, and the children through the influence of the visiting nurse or by other means be subjected to the Pirquet test to determine what relationship, if any, might exist between the occurrence of sputum on the street and a positive skin test among the children.

I have mentioned what difficulties we have had in trying to find tubercle bacilli outside the body in a health resort and how our results for certain eating utensils were positive. It is interesting to note in regard to this that but one case of tuberculosis developed in any of the employees at the Trudeau Sanatorium during the thirty-six years of its existence. This case, one among many hundred employees, could easily have been contracted elsewhere and has never interfered with the woman's working ability. It was so slight that we might class it as doubtful.

The feces of all patients with tubercle bacilli in their sputum may be safely said to contain living tubercle bacilli. Whether they are excreted in the bile through the liver or come, as most probably do, from the swallowed sputum, is for our present purpose immaterial. The sewage of Saranac Lake empties into the Saranac River below the village. Mr. Petroff, Dr. Heise and I found tubercle bacilli at all levels of the river at the sewer's mouth but they grew less, as the mouth receded, to disappear at a distance of about four miles down the river, which flows about two to four miles an hour. It is hardly conceivable that under such conditions sewage contamination can play any important part in the production of tuberculosis.
To sum up our work, we have found tubercle bacilli on the eating utensils that are introduced into the mouth, on objects kissed, in particles of sputum coughed out, on the dust of floors on which patients have spat and in sewage. Gross contamination of hands, through wiping the lips or soiling with sputum, may be transferred to others, but has not yet been proved. It is not, of course, fair to draw too broad conclusions from a study of the habitat of consumptives trained in good hygiene and to apply it to the general population, where all rules of prophylaxis may be broken through ignorance or on account of weakness.

The virulence of the tubercle bacillus has been much dwelt upon by many writers. Largely irrespective of the number of bacilli, they say, the virulence may determine the type of disease. It is interesting to note, as Theobold Smith has pointed out, that very virulent tubercle bacilli may kill the infected individual so quickly that this strain of tubercle bacilli is destroyed, as it cannot escape from the body. On the other hand, a weakly virulent type may also fail to effect escape from the body, as no open disease is produced, and so remains imprisoned. These factors would tend in a broad way to equalize the virulence of tubercle bacilli in chronic pulmonary tuberculosis. But even a slight variation in virulence may be sufficient to make effective a superinfection, though it must be remembered that artificial reduction of virulence is due more often to reduction of the number of the living tubercle bacilli. I know of no one who has intentionally reduced the virulence of a tubercle bacillus and kept it reduced. The resistance of the host to the tubercle bacillus and the accidental location of disease has unquestionably more to do with the type of disease than variations in virulence.

Recently Brownlee has suggested that his studies lead him to believe that pulmonary tuberculosis is a mixture of several types of disease due to different strains or types of tubercle bacilli. It would appear that opportunities for infection, stress of life at different periods and environment, are strongly complicating factors.

Three types of human tubercle bacilli have been separated by Petroff and it is possible that further knowledge may be gained by study of these and their correlation with the type of disease.

The number of bacilli on the other hand has a marked influence on disease. While a few may produce only infection or a slight superinfection, many may produce acute disease. Acute tuberculosis is often the result of an accident. A small area, a focus, of disease becomes crowded with tubercle bacilli and breaks into an artery or vein or lymph...
duct. An acute pulmonary or generalized tuberculosis may result. No one is so immune that a sufficiently large number of tubercle bacilli will not produce infection and ultimate disease.

Evidence can be adduced to prove that practically every possible, or impossible, method of infection that has been so far suggested, is not the usual one. Flügge had much difficulty in finding tubercle bacilli in the dust of streets or rooms and Cornet in turn attacked his droplet method, for coughing into the faces of animals does not seem to infect them with any degree of certainty, and yet 30 of 76 guinea pigs, kept in cages in wards with consumptives, became tuberculous. Bovine bacilli play some part in childhood infection but none in pulmonary tuberculosis in adults, unless we accept mutation, that is, that bovine can change into human tubercle bacilli, which no one has proved. Human bacilli may be carried from man to man by the slight infection imparted to them by the hands, but this seems unlikely, for we know that particles of dried sputum do not rub off easily and tubercle bacilli in thin layers are quickly killed by light and air. Hand-to-mouth infection is probably far more common than hitherto considered, and utensil-to-mouth infection cannot be ignored. Summing up the various methods of infection, it seems to me unwise to stress any one too heavily. Milk must be produced by nontuberculous cows or else pasteurized before use. Greater care must be given to the disposal of tuberculous sputum. The mouth must be covered with a piece of cloth during cough and stricter attention must be paid to rendering eating utensils, that approach the lips, sterile after use. From this the importance of strict hygienic measures for the patient with tubercle bacilli in his sputum, whether incipient or advanced, cannot be overemphasized. For the poor, hospitalization seems to offer the best means of preventing infection while the reporting of all cases is consequently of equal importance.

THE HOST

So far we have considered etiology from the standpoint of the tubercle bacillus. It is inconceivable that the host has no influence upon the development of disease, though upon primary infection it may exert little.

It is well known that children, healthy or weak, are nearly all susceptible to certain infections, for example, measles. To-day we are forced to believe that the same condition holds true for tuberculous infection; for, while possibly only 70 per cent of all individuals react to tuberculin
at the age of puberty, thus proving that they harbor or have harbored tubercle bacilli in their bodies that have produced tubercles, several observers hold that all have a tuberculous infection before death while some affirm that this is so at the twentieth year. The movement of the people from the country to the cities, from where the population is sparse and relatively isolated to where it is dense, has certainly greatly facilitated infection, which some would have us believe is one of the true causes of the decrease in tuberculosis mortality. From this we may assume that, so far, all our methods of prevention have affected only massive infection, or have so raised the resistance of the more slightly infected that they hold their infection in a dormant state or, what is less likely, eradicate it.

This primary infection may occur with slight or indeed with no manifestations of ill health save a slight indisposition for a few days, though Pirquet believes that before the age of two years infection is usually manifested by some clinical symptoms, such as bronchitis. It is of interest to recall here how little influence a primary inoculation exerts upon the general health or at the site of injection in experimental tuberculosis. Stress has been laid upon what slight exposures are followed by primary infections in infants and young children. There can be no question that young children and primitive races, not hitherto exposed to tubercle bacilli, react very differently and much more acutely to infection with the tubercle bacillus than do those past puberty in the civilized races. The lymph nodes and tissues seem after the third year to offer a less favorable soil for the growth of tubercle bacilli. It is well recognized that the lungs also suffer at this age; but after puberty the lungs bear the brunt of the attack, and furnish what may be called the adult type of tuberculous disease which, however, can exist for years even when fairly extensive, and attract no attention.

Tubercle bacilli may enter the body (1) through the eyes, gaining access to the pharynx through the tear duct, (2) through the nose, and (3) through the mouth. Entrance through the skin can be disregarded for our present study. All three portals of entry converge in the pharynx and may lead to infection through the tonsils, as Crowe has shown, and through other masses of lymphoid tissue well distributed throughout the upper respiratory tract. Recent work has shown that inhaled bacteria can be recovered in the ultimate division of the lung, the air cells. Again, the tubercle bacilli may be swallowed and enter the body through the intestines which Calmette has recently emphasized and Theobald
Smith questioned. It would lead us too far afield to discuss here these modes of entry; but in an uninfected person the tubercle bacillus can pass through the slightly injured or normal mucous membranes, enter the lymph stream, pass into the blood and be filtered out in the small blood vessels and capillaries. They may lodge for a time in the case of the lungs in the lymph masses, but before long are transported to the lymph nodes about or near the roots of the lungs. Here they reach a final resting place and produce more or less tuberculosis. This area of disease, though it may be very small, is large enough to produce certain changes in all the cells of the body, which hereafter react to the tuberculin tests, though its effect upon the person may be so slight that he is hardly aware of it. His cells thus become sensitized to the tubercle bacillus, and when the latter again gains entry into the body or escapes from its primary site, it may be attacked more vigorously. It seems most likely that several portals of entry may be used at the same time or one after another by the different reinfections that are constantly occurring.

Chronic pulmonary tuberculosis is of extreme rarity in early childhood. In fact, some have held that a clinical diagnosis of tuberculosis during the first year of life spells death; but more recent figures show that even during the last three months of this year the prognosis is somewhat less fatal and that some resistance has been acquired. More deaths from tuberculosis occur during the first year of life than during any other (Hess) due, no doubt, to frequent reinfections with large doses of germs from tubercle bacilli carriers who fondle the babies. During the first two years of life the child is subjected usually only to the degree of infection present in the home and about 10 per cent are infected. If "home" infection is present it is possible that the infection may be severe and death more likely result. Even at this age the lungs rarely escape.

The bearing of these facts upon etiology is clearly evident. The infant and young child cannot be guarded too carefully against infections. In the household of the open case of pulmonary tuberculosis extreme care should be practised. If the mother has an open tuberculosis when the child is born it should be removed from home at once, and thus 97 per cent may escape infection, or else if at all possible kept apart from its mother. She should never nurse it. It is impossible, however, at this time to go further into the minute details necessary for the protection of young children in these households.
Up to the third year only 15 to 20 per cent have been infected. After this age, when the child begins to toddle about and make longer or shorter excursions into the outer world, opportunities for infection greatly increase, and infected toys, infected hands, infected spoons, as already described, may play a much larger part in primary infection than many have hitherto held. During the next four years, that is, from the third to the seventh year, 40 per cent of children are infected according to some statistics. Curiously, while the number of children infected increases with age up to puberty, the mortality decreases. If perchance a tubercle bacillus carrier, an open case of tuberculosis, is present in the house with a child under three years of age, infection takes place almost without exception, and tuberculous disease is much more likely to result from such extensive or repeated reinfections, though many still escape. Pearson has shown that the parent is twice as dangerous for the offspring as the tuberculous husband or wife is for the well member of the couple. This is another way of stating the fact that not only infection but disease is more likely to incur in those who are exposed early in life. However, Pollak found that after four years of age the entrance of a tuberculous patient into the family affected the child little, if at all; but, if introduced before this age, the child either grew up more delicate than its older brothers and sisters or if under two years of age was almost surely infected (96 per cent). Bergmann had no children die who were exposed after four years of age. In a study by Lampson 2 per cent of the family group without any tuberculosis gave a positive cutaneous tuberculin test, 22 per cent if latent tuberculosis was present, 67 per cent with open tuberculosis and 33 per cent with healed tuberculosis.

**BOVINE INFECTION**

When Detre announced (and by so doing is said to have won his bride) that individuals infected with bovine tubercle bacilli reacted more to tuberculin made from bovine tubercle bacilli than to that made from the human type, it was thought that a great step forward in the etiology of tuberculosis had been taken, but unfortunately no verification of this has been forthcoming. From the figures previously given it is seen how readily children might become infected by tuberculous milk when the exposure, though slight in amount, is so widespread. Krause has pointed out that the amount of childhood infection increases as soon as the child is able to walk, or in other words when he begins to play upon
LAWRASON BROWN

the street. He affirms that at this time the child drinks less cow's milk but it seems to me this is also the age at which less attention is paid to his milk, and it is also an age not so far removed from the time when he ceases to be breast fed. He has not excluded, it seems to me, the danger of infection by bovine tubercle bacilli, for many children consume much cow's milk from the age of three to seven. It is possible then that some of the infections that occur between these ages may be due to bovine tubercle bacilli. After puberty, bovine tubercle bacilli, which cause about 25 per cent of the disease up to this time, appear no longer able to produce much disease; for of a large series of cases investigated after this age, only 1.3 per cent had disease due to the bovine type and less than half of these were pulmonary disease. It is of interest to note that when all exposure to open tuberculosis can be excluded, 25 per cent of the children still react (Hillenberg, quoted by Roemer). Even inoculation of adults with virulent bovine tubercle bacilli seems to produce slight infection and apparently no disease. Many cases of tuberculosis of the glands of the neck, due to bovine tubercle bacilli, are either stationary or very slowly progressive. Some would explain such observations by stating that before the bovine germ is ingested, nearly everyone is infected and vaccinated with the human tubercle bacillus, a statement which is contrary to fact.

It appears impossible to-day to decide to which type of tubercle bacillus the majority of early infections are due. Into the homes where no carriers live the bovine tubercle bacilli come without doubt more frequently than the human type, but the youngerster of three to seven years of age must have ample opportunity for infection while at play upon the street.

It would seem then a wise procedure to guard our children against tuberculous milk, and the provisions should be stricter the younger the child. For adults, unless the milk be very severely infected and undiluted with normal milk, the danger is negligible. The tuberculous cow should be excluded from all dairy herds but may be used for breeding purposes. It has been suggested that bovine infection protects against infection by the human type, and that it would be an unwise procedure to eradicate bovine tuberculosis. It has been advanced by Brownlee that his "middle age" type of pulmonary tuberculosis is closely associated with tuberculosis in children under five, and he implies that early tuberculosis in children, possibly bovine in origin, immunizes them against pulmonary tuberculosis in early adult life. But the resistance of the
infected child may be at low ebb, the strain of the germ may be more virulent, the repeated doses may be massive, and so defeat our purpose. Instead of vaccination we may have to face disease. Such protection therefore is to-day too far from being proved to permit us to suffer a disease to continue to exist, which causes 10 per cent of all the deaths and at least 15 to 20 per cent of all the disease due to tuberculosis in children. It must be recalled, however, that tuberculosis is very common where bovine tuberculosis does not exist, and where cow's milk is never used for food. However this may be, I still hope that we may yet be able to inject a vaccine of bovine tubercle bacilli into man that will render him immune to human infection. Calmette claims that his strain of bovine tubercle bacilli, grown upon a potato medium, glycerinized and treated with ox bile, is not virulent for cattle and that in doses of at least 44,000 injected intravenously, it is nonvirulent for man.

HEREDITY

The tendency in tuberculosis work since the time of Villemin has been to emphasize infection more and more, and to belittle that unknown and mysterious factor, heredity. Some years ago Mr. Pope and I began a study of heredity but soon abandoned it as we saw no opportunity with the data at hand of arriving at any definite conclusion. That so called phase of heredity, the intrauterine infection of the child, is so rare, and the child succumbs so quickly that we need not consider it as of any practical importance. It is questionable how far, if at all, constitutional or hereditary factors prevent a first infection; but it seems to me that they may play a very important part in the development of disease from the primary infection or in the resistance to reinfection. For example, an ability to form tubercles may be entirely lacking as in white mice, or greatly lessened or indeed increased. Again the ability of the organism to react by the rapid and sufficient formation of fibrous tissue may be passed on in certain strains of the human organism. Tuberculoprotein hypersensitiveness can be inherited from a sensitive mother, but is inconstant and is probably never handed down to the third generation. The inheritance of certain physical peculiarities cannot be denied, and it is possible that after infection certain inherited characteristics may lead, on the one side to increased and, on the other, to lessened resistance and so to a less or greater tendency to frank disease. This has not been conclusively proved, though the work of Pearson and of Pearl is strongly suggestive. I can see no reason why certain families, if acquired char-
acteristics can be transmitted to offspring, should not develop an ability to react with increased resistance, and King and Reibmayr affirm that children of tuberculous parents do. Under other conditions a liability to catarrh, or even to structural changes that favor infection may be inherited. Turban, Baldwin, and Strandgaard attempted to prove that pulmonary susceptibility was inherited in certain families in regard to point of origin of the disease in the lungs, its general course, and the age at onset. The small number of their observations do not lend them great weight.

The appeal to medical work published before the discovery of the tubercle bacillus as some (Bullock and Greenwood, and Bushnell) have done, does not bear much weight, for many of the predisposed, with fair, white skin, flushed cheeks, soft and slender muscles, have probably already been infected, and their development in some way arrested. Here the tubercle bacillus may be or is the cause of the predisposition.

The inheritance of predisposition to pulmonary tuberculosis is, Pearson and others affirm, just as likely to occur as the transmission of normal physical characteristics or as insanity and deafmutism. The relationship between husband and wife in regard to pulmonary tuberculosis is far less close, and so indicates that infection is not the chief factor, for where selection of mates is freer, for example, among the middle classes, the relationship is closer than among the poor. Infection and acquired resistance, as Cummins has pointed out would, however, explain this as well as heredity.

Race has unquestionably some relationship to the mortality from pulmonary tuberculosis. It has been found that more children among the Italians than among the Irish react to tuberculin but more Irish than Italian adults die from pulmonary tuberculosis. Here again racial temperament and infection complicate the study. Apparently savage races, as well as negroes and American Indians, show a lessened resistance to pulmonary tuberculosis.

The whole question is greatly complicated by the fact that slight early infection increases resistance to the tubercle bacillus, and some would affirm that this is the more plausible assumption (Cummins). The reaction to the tubercle bacillus of savage tribes who have never come in contact with the tubercle bacillus is no argument against a tuberculous diathesis, for, as Pearson has pointed out, such races may include many families with less natural resistance to the tubercle bacillus than others. Then again lack of all hygienic conditions makes massive infection from a tubercle bacillus carrier the rule.
If the host can react to the tubercle bacillus, it is also possible for the parasite to react to the host, as Dr. Welch pointed out in his Huxley lecture in 1902. The whole theory of exotoxins, that is, poisons given off from the living germ, is associated with the reaction of the parasite to the host. Another point of interest is the question whether such a reaction may lead to greater powers of resistance on the part of the germ, and so enable it to repel better the attack of the same strain of tissue. I mean by this that a tubercle bacillus which has successfully overcome the resistance of one offspring may prove of greater danger to another offspring of the same father and mother than one not so related. Parental infection, according to this, would not be as dangerous as infection of offspring by offspring. There are no data on which to base this assumption, and accordingly no especial reason to forbid members of a family from nursing one another.

In any case the question is not, as Pearl says, whether all disease is due to constitutional factors alone or to environment alone but how much influence does each factor exert in the development of the disease. The question is still unsettled, and I hope that Pearl's work now under way will help much to clear this vexatious problem.

SUPERADDED INFECTION

Reference has been made to reinfections in the same individuals, and here again we are much at odds. Several years ago Behring stated that all tuberculosis was due to bovine infection, which was acquired early in life, remained latent during childhood, and only later in life developed from infection to disease. Much work has disproved this. A well known worker in tuberculosis wrote some years ago, "Childhood is the time of infection, youth the time of superinfection, and that from extension of the primary disease." This would of course exclude adult reinfection, and would render any man or woman with a positive tuberculin reaction ordinarily immune to tuberculosis. The importance of these views in the antituberculosis campaign is very evident. Only individuals who have been infected should engage in tuberculosis work for they, it would imply, are safe from further infection but, on the other hand, just as liable as others to the development of disease from the primary infection. In fact, any one who reacted to tuberculin could pay little heed to further infection from without but much to the avoidance of debilitating circumstances.
THERE IS NO REINFECTION FROM WITHOUT

Many arguments have been advanced to show that adult reinfection rarely, if ever, occurs, and that pulmonary tuberculosis is the development of childhood infection. We have said that 70 per cent of individuals have had tuberculosis in their bodies by the age of puberty, and some affirm that all are infected by the age of thirty. Infection occurs much more easily in early life. Apparently normal lymph nodes may contain living tubercle bacilli which are found at times even in completely calcified areas of former disease. Pulmonary tuberculosis follows more often depressing influences than any recent exposure to infection. Close association in adult life causes apparently little increase in mortality of those so exposed. The fact that the lungs are chiefly affected in adult life may be due to the fact that injuries are less frequent than in childhood, and that the lungs are the great filter for any germs that escape into the circulation.

Some have suggested that reinfection from without is less likely to occur when the resistance is lowered; for the tubercle bacilli in the body have already adapted themselves to the host and consequently the usual reinfection would be from within. If the tubercle bacilli can adapt themselves to the host, it is also possible for the host to develop greater powers of resistance against this primary strain. Such reasoning is of course hypothetical, and Roemer could detect no difference in reaction in guinea pigs by inoculation of the skin. Infection from within is clearly the most common method of progression of the disease in experimental tuberculosis and of its spread to the lung, though reinfection from heavily contaminated feces and urine may be conceived. Roemer himself showed that only when very small doses were employed did animals fail to become superinfected, and not only the number but the virulence may overcome this resistance in man.

Tubercle bacilli unquestionably long lie dormant in tissues apparently normal, though some claim more careful study would reveal microscopic disease; but it is difficult to see why doses sufficient to produce disease later in life, which some hold must be "massive," do not produce disease at the time of infection early in life when the body is more susceptible to the tubercle bacillus.

In a recent important and timely book Bushnell has attempted to show that only massive infecting doses, such as very rarely if ever occur in the life of man, can cause a reinfection from without. He assumes
that every individual who harbors tubercle bacilli may excrete them at times through his intestine. He also assumes that the vaccination from childhood infection persists throughout life, which we know is not true for calves and cattle. Tubercle bacilli which escape into the blood stream, he says, cause no new areas of disease. He quotes the experience of Lippspringe, where, with enormous numbers of consumptives (8,000 per year in 1906–1909), crowded into narrow quarters with the natives, taking no special care of the sputum for many years, the tuberculosis mortality fell from 98 per 10,000 in 1831–1840 to 35 in 1906–1909. The population was 1440 in 1830, and 3472 in 1909. So, he argues, quoting Werner, that the contagionist's view as to the high infectiousness of pulmonary tuberculosis is false. In Schlanger the same was true. It is of some interest to recall that for ten years no native in Saranac Lake (population about 5000) died from pulmonary tuberculosis, and the high death rate quoted in these two health resorts appears to suggest that either the death rate among children was excessive, or that the bad hygienic conditions fanned childhood infection into adult disease or that adults were reinfected. The argument is advanced that patients with malaria or syphilis are immune to further infections, and so by analogy a second reinfection with tubercle bacilli is not possible. This assumes that tubercle bacilli once in the body never die, for if syphilis be cured a second infection readily takes place. That the tubercle bacillus never dies has not been shown, and cattle experiments controvert this view. According to this view, the worst thing that could happen to a patient with pulmonary tuberculosis would be to recover entirely.

Some years ago Mr. Pope and I attempted to prove infection. We collected 40,000 married couples, one of whom was tuberculous, both of whom were dead, and so, by excluding any connecting hereditary taint, hoped to arrive at some estimate of the danger of infection from husband to wife or vice versa. But even here "assortative mating," that is, that persons with the same physical and mental tendencies are more likely to marry, enters and complicates the situation. There was definite evidence of infection but two-thirds of this was thought by Pope and Karl Pearson to be due to assortative mating. If one wishes to deny this influence there is definite evidence of infection, though not great, of one consort by another. Most of the recent statistics on this fact are of small value as one, the healthy, or often both, of the parents are still alive. Though here too another difficulty enters, for some of the well spouses may develop tuberculous disease, and recover from it, only to die of nontuberculous disease.
Attention has been drawn by Hess to the fact that deaths from all forms of pulmonary tuberculosis increase very markedly at thirteen in girls and at sixteen in boys or, in other words, at puberty, which he thinks is the determining cause of this increase. He then states that if this is due to infection, such infection must have been continuous, which he disbelieves though he refers to "tubercle bacilli shedders." He advances this as an argument against reinfection from without and in favor of reinfection from within. It could also be used as a demonstration of change or decrease of immunity at puberty which favors reimplantation of tubercle bacilli from without.

Newsholme has pointed out that figures quoted from hospitals for the tuberculous when carefully analyzed may show that reinfection has occurred. The same holds for other figures (Freymuth).

**REINFECTION FROM WITHOUT OCCURS**

On the other side are many facts that suggest that reinfection from without may play a very important part in many cases. Krause has shown experimentally that a primary infection by the vein in guinea pigs leads to the temporary presence of tubercle bacilli in the lungs. A second infection by inhalation produces a very different picture for here the tubercle bacilli are "fixed" in the lungs which react severely, and in certain immune animals the tubercle bacilli are destroyed apparently in time. In those individuals who have lost in large part their immunity or in whom the dosage is too large, no such retrogression occurs, and infection is followed at once by disease.

It is also of interest to recall that Winternitz, from a study of poisonous gases, is led to conclude that the portal of entry of bacteria into the lungs is through the air currents which may finally deposit the germs in the ultimate recesses of the lungs. It has long been known that of all natural methods of infection, that by inhalation requires the smallest dose. Even avirulent tubercle bacilli, when sprayed into the faces of guinea pigs, cause the formation of tubercle in the lungs, tubercles however, which may ultimately disappear. This, of course, would explain what happens to many pulmonary infections in adults. It is also very suggestive that reinfections of guinea pigs by the vein does not lead to such a marked formation of pulmonary tubercles. The experiments that show that reinfections can occur in animals are numerous. In fact, Roemer, one of the great opponents to reinfection, had to use very minute doses of tubercle bacilli or he would reinfect his animals. In
some experimental work certain bacteria caused pneumonia only when sprayed into the air passages, and not when inoculated. It is of interest also to note that it is very difficult to infect rats by inoculation but comparatively easy to do so by the aerial route. We must bear in mind the fact that a primary infection by a moderate number of tubercle bacilli leads to involvement of the nearest (regional) lymph glands, while a secondary infection does not involve these glands. The work of Opie has convinced him that two types of tuberculous lesions exist in the lungs, one occurring anywhere in the lungs, not fatal, but often healed, and associated with involvement of the lymph glands; the other in the apex of the lung, often fatal, and not associated with involvement of the lymph nodes. The latter, he holds, is modified by the primary infection, though due to a slight infection which he implies, I take it, is from without.

From figures collected by the Imperial German Bureau of Health, in a study of 1400 cases with reference to the occurrence of human and bovine tubercle bacilli, it was found that 50 per cent of the tuberculosis of the abdominal lymph nodes, 41 per cent of the lymph nodes of the neck, 23 per cent of general tuberculosis, and no cases of pulmonary tuberculosis where due to the bovine bacillus in children, where the infection is almost certainly due to imbibed milk. Adult pulmonary tuberculosis is due to the human type in 99.3 per cent of all cases, where the disease is manifest, and it is of interest to compare these figures with those where the infection is known to be by ingestion. It implies to me that infection through the respiratory tract is often the cause of pulmonary tuberculosis, and that possibly in a larger number of cases than many would like to admit the cause of pulmonary tuberculosis is direct infection of the lung. Opie's recent work on British and American soldiers would suggest that infection (or reinfection?) by ingestion might preclude pulmonary disease.

Ward in a study of rural tuberculosis in England comes to the conclusion that adult infection does occur. In 252 cases, he attributed 40 per cent to immediate infection, 19 per cent to remote, 10 per cent had only a doubtful contact and 31 per cent no discoverable contact. In 96 children, 74 per cent were immediate, 2 per cent remote, 1 per cent doubtful and 23 per cent negative. He investigated 102 nontuberculous control cases and found 5 per cent exposed to immediate, 7 per cent to remote infection, 6 per cent to doubtful, and 82 per cent to none. A study of 77 tuberculous soldiers showed 5 per cent immediate, 26 per cent remote, 2 per cent doubtful and 67 per cent negative exposure.
The argument, that never in adult life is the infecting dose of tubercle bacilli large enough to bring about reinfection and disease, can be opposed by the statement that a series of reinfections, each of which is small in itself, may aggregate in the whole a fairly large dose. None deny that massive infection from without can produce disease in adult life. Some who deny reinfection emphasize the importance of tubercle bacillus shedders, which they say, play a large part in primary infection, but none, they imply, as sources of reinfection. Another interesting fact is that adult pulmonary tuberculosis is almost always situated at the periphery where inhalation infection would explain it, while childhood infection most often arises around the roots of the lungs. In the cases whose tubercle bacilli in the primary infection are well walled off, debilitating conditions can be supposed to arise which might lead such foci to act like loci minoris resistentiae for a superinfection from without, while still preventing infection from within. The whole thing seems to be a matter of the balance of resistance and dose and possibly virulence.

The experience with immunity in cattle is of interest in this connection. Without going into detail, it may be recalled that calves can be immunized by the injection of human tubercle bacilli, and when placed in a cow barn with tuberculous cows remain well for many months; but after two years many, if not most, of them develop pulmonary tuberculosis due to the bovine germ. Either one of two things has happened; first, the human tubercle bacillus has been changed into the bovine or, second, a secondary infection has taken place from without, and disease has resulted. The transformation of one type of tubercle bacillus into another has never been observed and we are forced to accept the latter explanation. Calmette's recent work with bovine tubercle bacilli has also upheld this conclusion.

Deaths from tuberculosis occur least frequently between the ages of ten and fifteen. From this time on the mortality from tuberculosis increases, and the lungs are the organs most frequently attacked. After this age the bovine infection, which was fairly frequent before, now becomes, so far as the lungs are concerned, almost negligible. Previous reference has been made to the possible changes that occur in the body at this time and their possible bearing upon the bovine tubercle bacillus. It has seemed to me possible that many of the tuberculin reactions in the skin that occur early in life may be due to infection by the bovine tubercle bacillus for the reasons already mentioned. About puberty many of these infections probably become quiescent or die out entirely.
In fact, bovine tubercle bacilli, virulent for rabbits, have been inoculated subcutaneously into men, some of whom were tuberculous, but in none of the fourteen instances did anything more than a local abscess ever develop. Bovine tubercle bacilli are more susceptible to light and drying than human. It is also conceivable that infection by greatly weakened tubercle bacilli may bring about immunity, though in time they also may gradually weaken and die. From this time on the immunity which has apparently existed from the eighth or ninth to the fifteenth or sixteenth years begins to decrease, and from the twentieth to the thirtieth years the decrease is very marked, if increase of mortality is an indication.

Personally, I do not believe that all the immunity reactions are lost; for I believe that cellular immunity outlasts by far any of the humoral indications that we have. It seems to me that we must in our intercourse with the world come in frequent contact with the human tubercle bacillus, and as we grow older it is probable that infected objects play a smaller part in our reinfections. Inhalation infection requires far fewer tubercle bacilli than ingestion, and it seems to me possible that sooner or later all of us breathe tubercle bacilli into our lungs. Where the cellular immunity persists the tubercle bacilli are probably attacked and localized in the first mass of lymph cells they reach. I do not believe that many of these infections “take,” that is, develop into disease, but sooner or later some do, and the resulting pulmonary tuberculosis is due to this secondary infection occurring from without in adult life. This does not mean that the reinfection may not lie dormant for a long time, for in many instances I believe it does. Nor would I deny that tubercle bacilli entering the body through the upper respiratory tract or elsewhere may not reach the lymph vessels, and passing through the blood find a lodging place in the lungs, there to act similarly to those inhaled. I am inclined to believe that 50 per cent of all adult pulmonary tuberculosis is due to reinfection after puberty. Reinfection is probably less frequent after the third decade. For these reasons it seems to me that the care of the patient with advanced pulmonary tuberculosis is very important in the eradication of adult pulmonary tuberculosis on account of this danger of superinfection.
FACTORS THAT FAN INFECTION INTO DISEASE

That reinfection can occur from within cannot be denied. Complications arise in organs not exposed to direct infection from without. Clinical relapses occur and the areas of disease spread both to the same and to the opposite lung. Symptoms arise for the first time in disease of the lung which both physical signs and X-ray plates show is of long standing. Trauma also causes apparently new localizations of the tubercle bacilli and tuberculous disease which did not previously exist, but affects pulmonary tuberculosis but little. The strain of pregnancy lights up not only known disease but brings to light unsuspected disease in women hitherto apparently healthy. Measles acts in a similar way, and some hold the same is true for the common colds and influenza. Whether pulmonary tuberculosis results from reinfection from within from a primary childhood infection or from an adult reinfection from without, it is probable that more or less time elapses between reinfection and clinical disease. This latent period may vary from a few weeks to many years; for it is a question how soon, if ever, some tuberculous infections die out. (Some hold that even acute tuberculosis is always due to reinfection.) The fact that the vast majority of all adults have been infected, have been able to hold the pathological changes thus produced in abeyance, indicates that they have some resistance, and it therefore becomes very important—I cannot stress it too much if all of us become infected—to know what untoward circumstances upset the balance in favor of the body and turn the scale to favor the germ.

The development of infection into definite clinical pulmonary tuberculosis may be due to any debilitating circumstance. Recently, it has been pointed out that lack of sufficient food has increased the mortality from tuberculosis in Germany, until it has risen to what it was twenty to thirty years ago. It would appear from this that increased wages which would provide better food would also decrease the amount of pulmonary disease and the number of cases that die from it. Too little use of milk as a food is also an important factor.

Dusty trades have been much studied recently, and some have come to the conclusion that only certain dusts are of much importance, depending upon the character of the individual particles, and upon the chemical composition. Sharp, angular particles of dust, metallic or mineral dust, are much more dangerous than street or organic dusts. Gardner has found tubercle bacilli more frequently in the lungs of guinea pigs.
which had inhaled granite dust than in the controls, but the "dusted" animals had a longer life. Colds are a frequent precedent of the development of clinical pulmonary tuberculosis, and it has been suggested that adsorption of certain antitryptic ferments by the bacteria circulating in the blood during these infections might bring about this condition. Measles and influenza affect for a time the sensitiveness of the body, and some think in this way favor the spread of infection into disease. Repeated pregnancies and lactation are held to do the same thing, not only for cows, but for women as well. Indeed a single pregnancy at times appears to cause clinical pulmonary tuberculosis. Diabetes also predisposes to clinical disease.

In another large class fall all those conditions that we feel prevent the recovery of patients with pulmonary tuberculosis. These may act to change quiescent infection into active pulmonary disease. Change from an outdoor to an indoor life is bringing down many of our boys who fought in the war. Severe physical exertion acts only when the thread of resistance is nearly broken. Poor housing, insanity, dirty quarters, may also favor infection from without, but Todd, who has studied the situation in Chicago, feels it is difficult to prove by statistics the direct relation between tuberculosis and house. Chicago, he believes, contains more small bedrooms than any other city. The Italian blocks have more opportunity for crowding in small bedrooms but less crowding occurs than in Polish blocks, and yet have more tuberculosis. Curiously he finds more tuberculosis in blocks where children are fewest. The economic environment in the house, the use made of the house, and other factors, not as yet studied, for example, the history of the occupants of a single house over a term of years, all enter into and disturb any conclusions. Hence the term "house disease" must be applied to tuberculosis with caution. I would refer any one interested in this subject to the bibliography compiled by James Ford (American Journal of Public Health, vol. x, 1326).

Pulmonary tuberculosis is closely connected with the general death rate, and often rises and falls as it does. Poor general sanitation, particularly where bad water supply favors intestinal diseases like typhoid fever or where intestinal parasites are frequently found, all produce apparently more pulmonary tuberculosis.

It must not be forgotten finally that inability to take needed rest, too long hours of work, particularly in poorly ventilated rooms, inability to relax or to play, or again too hard play after long hours of work, burning
the candle at both ends, all cause pulmonary tuberculosis to spread in extent and can fan into existence an all but eradicated infection.

The whole subject of the etiology of pulmonary tuberculosis is still far from settled. I shall offer no conclusions to what I have said. All of us have our eyes fastened on this school of hygiene, hoping it will lead us into newer, clearer conceptions of the causes of pulmonary tuberculosis, and so enable us to bring about a great reduction of this disease, which to-day takes so large a toll of mankind at its period of greatest efficiency.